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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,103	02/14/2005	Steven Gareth Griffiths	N079 1150 US	5430

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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,103	GRIFFITHS ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-8,17,31-33 and 35-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-8,17,31-33 and 35-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/11/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/30/08 has been entered.

Claims 3-8, 17, 31-33 and 35-38 are currently under examination.

Claim Rejections - 35 USC § 112-2nd paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 3-8, 17, 31-33 and 35-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is vague and indefinite because it is unclear what is encoded by nucleotides 291-2153 of SEQ ID NO: 1. Is the sequence which encodes amino acids 162-365 of SEQ ID NO: 2? Figure 1 recites that the ORF of SEQ ID NO: 1 is nucleotides 291-2156. Accordingly, it appears that there may be an unintentional typographical error in amended claim 3 part (c). . Written support could not be found for nucleotides 291-2153 of SEQ ID NO: 1 (see also written description rejection below). Clarification and correction is requested.

Claim 17 is vague and indefinite because it is unclear what is encompassed by an open reading frame of SEQ ID NO: 2. Is this nucleotides 291-2156 as recited in Figure 1 or something else? The metes and bounds of the invention cannot be understood. Clarification and correction is requested.

Claim Rejections - 35 USC § 112-New Matter

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 3-8, 17, 31-33 and 35-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 3 recites the new limitation of "nucleotides 291-2153. Written support could not be found for nucleotides 291-2153 of SEQ ID NO: 1. Figure 1 recites that the ORF of SEQ ID NO: 1 is nucleotides 291-2156. Accordingly, it appears that there may be an unintentional typographical error in amended claim 3 part (c). Applicants must point to written support by page and line number for a nucleotide sequence comprising nucleotides 291-2153 of SEQ ID NO: 1 or remove/amend this limitation from the claim.

Claim Rejections - 35 USC § 112-Enablement

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 3-8, 17, 31-33 and 35-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "an isolated polynucleotide comprising the nucleic acid sequence set forth in SEQ ID NO: 1' or a full complementary sequence thereof', 'an isolated polynucleotide which amino acid residues 162 to 365 of SEQ ID NO:1; an isolated nucleic acid sequence comprising nucleotides 291-2156 of SEQ ID NO: 1 or fully complementary sequences thereof and a nucleotide sequence, or a fully complementary sequence thereof, which under stringent conditions hybridizes with the sequence of SEQ ID NO: 1 or its complement, wherein the stringent condition comprises washing for 1 hour at 55°C with 1 X SSC and 0.1% SDS, does not reasonably provide enablement for 'an isolated nucleic acid comprising nucleotides 291-2153 of SEQ ID NO: 1 or fully complementary sequences thereof. Vaccine compositions comprising any of the claimed expression vectors recited in claim 3 for the protection of any disease or methods of preventing any disease in a fish, including the diseases recited in dependent claims 36-38, are *not* enabled. Only vaccines comprising the VP2 when linked to the coding region of Hsp70 sequence were shown to provide protection against virulent IPNV (not any disease).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 3 recites the new limitation of "nucleotides 291-2153". Written support could not be found for nucleotides 291-2153 of SEQ ID NO: 1. Figure 1 recites that the

ORF of SEQ ID NO: 1 is nucleotides 291-2156. Accordingly, it appears that there may be an unintentional typographical error in amended claim 3 part (c). The specification does not teach or suggest any methods which utilize a vaccine comprising this region of nucleotides.

The instant specification at pages 24-25, Example 4, teaches that Atlantic salmon can be vaccinated intramuscularly with DNA expression vector/plasmids pUKrsxHSP70-ipnVP2 and pUKrsxHSP70-ipnVP3. The fish are challenged 4-6 weeks later by exposure to virulent IPNV (infectious pancreatic necrosis virus) and results indicate that "all of the nucleic acid vaccines based on the VP2 sequence of IPNV are protective against challenge by the virus, including the hsp70-VP2 fusion. The results do not state that the hsp70-VPN3 vaccines were successful. The results indicate that the VP2 sequence achieved protection against virulent IPNV when linked to the coding region of Hsp70, but are silent as to whether VP3 sequence has the same ability. Accordingly, only vaccines comprising pUKrsxHSP70-ipnVP2 and methods of protecting against disease caused by infection with IPNV (infectious pancreatic necrosis virus) are enabled. The specification does not provide any other working examples for prevention or protection against any other disease in fish (including Infectious Salmon Anaemia Virus, salmonid rickettsial septicaemia or bacterial kidney disease as recited in new claims 35-37), nor does it provide results with the use of any other DNA expression vectors, including solely an expression vector comprising SEQ ID NO:1, fragments thereof which encode amino acids 162-365 of Hsp70. The specification demonstrates that the coding sequence of Hsp70-linked to VP2 protein can protect against disease

Infectious Pancreatic Necrosis virus, yet the specification does not enable the use of Hsp70 and any other antigen to protect or prevent any of the numerous diseases that effect fish, including the ones recited in dependent claims 35-38.

Claims 31 and 32 are drawn to vaccines against any bacteria, virus, fungus, protozoa, nematode and tumor. It is unclear that the claimed Hsp70 nucleic acid sequences would have the ability to confer protection against *any* disease caused by any bacteria, virus, fungus, protozoa, nematode and tumor. The results provided in the instant specification and in the Declaration under 37 CFR 1.132 by Simard only enable the use of vaccines against IPNV (Infectious Pancreatice Necrosis Virus) through the use of VP2 and pET30 Hsp fusion. These results do not correlate to the use of ARthobacter HSP70 to protect against any variety of diseases caused by non-fish or fish pathogens as included in the scope of claims 31, 32, 33 and 35-37.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." The vaccine art is highly unpredictable and

therefore actual results from challenge experiments are necessary to enable vaccines and methods of prevention/protection. When considering a bacterial antigen as a vaccine candidate, three major considerations must be raised (1) the antigen must be conserved among strains of the bacterial species whose disease one wishes to prevent; (2) it must generate protective antibody such that the antibody to the antigen prevents disease; and (3) it must be a good immunogen such that protective antibodies are elicited in the population at risk and that these antibodies persist for sufficient time to provide protection throughout the risk period (Murphy et al. Pediatr. Infect. Dis. J. 1989. 8: S66-S68). Even when an antigen meets these three considerations, further testing often indicates that the antigen will not be effective as a vaccine. For example, Murphy et al. Pediatr. Infect. Dis. J. 1989. 8: S66-S68, teach that P6 is an important vaccine candidate based on these considerations, but Yamanaka et al (J. Pediatrics. 1993. 122(2): 212-218) later demonstrated that the population at most risk did recognize P6 as an antigen. The instant specification fails to demonstrate that the claimed DNA structures meet any of the three considerations known in the art to be important when considering a bacterial antigen as a vaccine candidate. Without specific guidance from the specification, it would take undue experimentation for those skilled in the art to make and/or use the claimed invention. Applicants should provide additional evidence, such as challenge experiments, to demonstrate these structures' ability as vaccines. There are no experiments which demonstrate that any of the claimed constructs could prevent ***any*** disease in fish (more specifically including Infectious Salmon Anaemia Virus,

salmonid rickettsial septicaemia or bacterial kidney disease as recited in new claims 35-37).

Given the lack of guidance contained in the specification, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Response to Applicants' Arguments:

With respect to the vaccines and methods of prevention, Applicants have argued that 'working' examples are not required. They argue that is within one of skill in the art to discover constructs which would have the ability to prevent any disease in fish (and, including Infectious Salmon Anaemia Virus, salmonid rickettsial septicaemia or bacterial kidney disease as recited in new claims 35-37). They argue that additional evidence by way of the Declaration of Nathalie Simard under 37 CFR 1.132 shows that Arthrobacter hsp70 protein has immunogenic activity in its own right and be the active principle for a vaccine to prevent or treat a variety of human and veterinary diseases. This has been fully and carefully considered but is not deemed persuasive. . The results provided in the instant specification and in the Declaration under 37 CFR 1.132 by Nathalie Simard only enable the use of vaccines against IPNV (Infectious Pancreatic Necrosis Virus) through the use of VP2 and pET30 Hsp fusion. These results do not correlate to the use of ARthobacter HSP70 to protect against any variety of diseases caused by non-fish or fish pathogens as included in the scope of claims 31, 32, 33 and 35-37. The test for whether an invention is enabled takes into account whether a disclosure would require undue experimentation and includes: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction

or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims. The bacterial vaccine art is highly unpredictable. As stated above, when it comes to evaluating methods of *prevention* of disease and *vaccines* in a highly unpredictable art, such as bacterial vaccine, the standard is high and specific examples are needed to support enablement. When considering a bacterial antigen as a vaccine candidate, three major considerations must be raised (1) the antigen must be conserved among strains of the bacterial species whose disease one wishes to prevent; (2) it must generate protective antibody such that the antibody to the antigen prevents disease; and (3) it must be a good immunogen such that protective antibodies are elicited in the population at risk and that these antibodies persist for sufficient time to provide protection throughout the risk period (Murphy et al. Pediatr. Infect. Dis. J. 1989. 8: S66-S68). Even when an antigen meets these three considerations, further testing often indicates that the antigen will not be effective as a vaccine. For example, Murphy et al. Pediatr. Infect. Dis. J. 1989. 8: S66-S68, teach that P6 is an important vaccine candidate based on these considerations, but Yamanaka et al (J. Pediatrics. 1993. 122(2): 212-218) later demonstrated that the population at most risk did recognize P6 as an antigen. The instant specification fails to demonstrate that the claimed DNA structures meet any of the three considerations known in the art to be important when considering a bacterial antigen as a vaccine candidate. Without specific guidance from the specification, it would take undue experimentation for those skilled in the art to make and/or use the claimed invention. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42

USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention."

The instant specification at pages 24-25, Example 4, teaches that Atlantic salmon can be vaccinated intramuscularly with DNA expression vector/plasmids pUKrsxHSP70-ipnVP2 and pUKrsxHSP70-ipnVP3. The fish are challenged 4-6 weeks later by exposure to virulent IPNV (infectious pancreatic necrosis virus) and results indicate that "all of the nucleic acid vaccines based on the VP2 sequence of IPNV are protective against challenge by the virus, including the hsp70-VP2 fusion. The results do not state that the hsp70-VPN3 vaccines were successful. The results indicate that the VP2 sequence achieved protection against virulent IPNV, but are silent as to whether VP3 sequence has the same ability. Accordingly, only vaccines comprising pUKrsxHSP70-ipnVP2 and methods of protecting against disease caused by infection with IPNV (infectious pancreatic necrosis virus) are enabled. This does not mean that VP2 is necessary; however, it also does not support whether VP3 possesses the same

ability. The results in the specification and presented in the Declaration are not commensurate in scope with the claimed invention.

Status of Claims:

It is noted that claims 3-8 and 17 are free of the prior art and would be allowable if the issues surrounding nucleotides 291-2153 in part (c), as outline above in the New Matter, 112 2nd paragraph and enablement rejections (2156 vs 2153) were obviated.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645